ANTIBIOTIC RESISTANCE INFORMATION CORNER

Multicenter, Postmarketing Assessment of Levofloxacin in the Treatment of Adults with Community-Acquired Pneumonia

B. Akpunonu, J. Michaelis, C. N. Uy, A. M. Tennenberg, B. A. Wiesinger, R. Karim, J. Scott Marshall, and J. B. Kahn. Clin Infect Dis 2004; 38:S5-S15.[1]

This large-scale community-based study confirms the results of previous studies that demonstrate the safety and efficacy of levofloxacin treatment for patients with community-acquired pneumonia. A 500 mg (once daily for 10-14 days) treatment of levofloxacin was effective among these patients and was also effective among those infected with *S. Pneumoniae* resistant strains to penicillin.

Multicenter, Open-Label, Randomized Study to Compare the Safety and Efficacy of Levofloxacin versus Ceftriaxone Sodium and Erythromycin Followed by Clarithromycin and Amoxicillin-Clavulanate in the Treatment of Serious Community-Acquired Pneumonia in Adults

C. Fogarty, G. Siami, R. Kohler, T. M. File, Jr., A. M. Tennenberg, W. H. Olson, B. A. Wiesinger, J.-A. Scott Marshall, M. Oross, and J. B. Kahn. Clin Infect Dis 2004; 38:S16-S23. [1]

This study compares the safety and efficacy of levofloxacin versus a ß-lactam/macrolide combination to treat seriously ill patients with community-acquired pneumonia (CAP). Treatment with levofloxacin was shown to be equally effective as ß-lactam/macrolide combination among CAP study patients. Study findings support recommendations of the empirical use of a ß-lactam/macrolide combination, or monotherapy with a respiratory fluoroquinolone (e.g., levofloxacin), for patients with serious CAP infections.[2] Further details and discussion of treatment regimens are provided in the article.

1. Articles available at: www.journals.uchicago.edu/CID/journal/contents/v38nS1.html
2. Mandell LA, Bartlett JG, Dowell SF, et al. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. Clin Infect Dis 2003; 37:1405–33.

Clinical practice guidelines and other resources:

In late 2001, the California Medical Association (CMA) Foundation AWARE Project began the development of its clinical practice component. The purpose of the Clinical Compendium is to provide tools and education resources to enable physicians and other healthcare providers to more appropriately prescribe antibiotics for acute respiratory tract infections. It was designed to summarize appropriate antibiotic treatment of common outpatient infections, and is based on guidelines and recommendations from leading medical experts and professional organizations in the U.S. The guideline looks at five uncomplicated respiratory tract infections: sinusitis, pharyngitis, bronchitis, acute otitis media, and viral upper respiratory tract infections. These diagnoses were selected because they account for 62% of all outpatient antibiotic prescriptions in the U.S. Adult and pediatric clinical antibiotic use compendiums are available at the web site below.

- The California Medical Association (CMA) Foundation — www.aware.md/resource/index.asp
- Clinical Practice Guidelines Compendium (Pediatric and Adult) — www.aware.md/clinical/clinical_guide.asp
- The Centers for Disease Control and Prevention — www.cdc.gov/drugresistance/community/
- The Los Angeles County Department of Health Services Acute Communicable Disease Control Program — www.lapublichealth.org/acd/antibio.htm
- Infectious Diseases Society of America — www.idsociety.org
- Clinical Practice Guidelines — www.journals.uchicago.edu/IDSA/guidelines/

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The following summaries stress the importance of judicious antibiotic prescribing. Acute otitis media (AOM) is the most commonly treated infection among children—over 5 million pediatric cases occur annually in the U.S. resulting in more than 10 million prescriptions. Between 40% to 75% of AOM cases are viral. Additionally, about 80% of children with AOM will recover without antibiotics and have no increased risk of serious infection. To address this, the American Academy of Pediatrics (AAP) and American Academy of Family Physicians (AAFP) recently published guidelines on appropriate treatment of ear infections.

Antibiotic Selection Pressure and Resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes*

Albrich WC, Monnet DL, Harbarth S. Emerg Infect Dis, Vol 10, No. 3, 2004.[1]

This study correlates outpatient antibiotic consumption with the prevalence of antibiotic resistant *Streptococcus pneumoniae* and *Streptococcus pyogenes* in Europe, North America and Australia. Total antibiotic use was significantly correlated with prevalence of penicillin-nonsusceptible *S. pneumoniae* (PNSP), as was macrolide use and prevalence of macrolide-resistant *S. pneumoniae*, and macrolide-resistant *S. pyogenes*. Among 20 countries in the study, U.S. data was only available for analysis in penicillin resistance and ranked high in the proportion of PNSP (34%), along with France (43%) and Spain (50%). The authors suggest that socioeconomic, cultural and behavioral determinants as well as healthcare policies have a major impact on outpatient antibiotic prescribing practices and resistance rates. These findings support efforts to promote appropriate use of antibiotics.

New Guidelines on Appropriate Treatment of Ear Infections

Subcommittee on Management of Acute Otitis Media (2004). Clinical Practice Guideline: Diagnosis and Management of Acute Otitis Media. American Academy of Pediatrics. American Academy of Family Physisicans.[2]

New clinical practice guidelines issued by the AAP and AAFP provide primary care physicians recommendations for the diagnosis and management of AOM in children 2 months to 12 years of age. These emphasize accurate diagnosis of AOM and address pain management with analgesics and to hold off on antibiotics. The option to observe and follow-up AOM cases for 48-72 hours can decrease unnecessary antibiotic prescriptions. In prior studies, the majority of parents were willing to treat their child's AOM with pain medication alone.[3,4] Summary recommendations from the guidelines are listed below.[5]

- Accurately differentiate AOM from otitis media with effusion, which requires different management.
- Relieve pain, especially in the first 24 hours, with ibuprofen or acetaminophen.
- Give parents of select children the option of fighting the infection on their own for 48-72 hours, then starting antibiotics if they do not improve.
- Prescribe initial antibiotics for children who are likely to benefit the most from this treatment.
- Emphasize prevention of AOM (i.e., encouraging breastfeeding, avoiding "bottle propping," and eliminating exposure to tobacco smoke).
- If antibiotic treatment is agreed upon, amoxicillin should be used for most children.

References

1. Article available at: www.cdc.gov/ncidod/eid/vol10no3/03-0252.htm
2. Guidelines available at: www.aap.org/ and www.aafp.org/x26481.xml
3. Cates C. An evidence based approach to reducing antibiotic use in children with acute otitis media: Controlled before and after study. BMJ 1999; 318:715-716.
4. Siegel R, Kiely M, Bien JP, et al. Treatment of otitis media with oberservation and a safety-net antibiotic prescription. Pediatrics 2003; 12:527-531.
5. American Academy of Pediatrics: Questions and Answers on Acute Otitis Media. Available at: www.aap.org/advocacy/releases/aomqa.htm

Clinical practice guidelines and other resources:

- The American Academy of Pediatrics - http://aappolicy.aappublications.org/
- The American Academy of Family Physicians - www.aafp.org/x132.xml
- The California Medical Association (CMA) Foundation - www.aware.md/resource/index.asp
- Clincal Practice Guidelines Compendium (Pediatric and Adult) - www.aware.md/clinical/clinical_guide.asp
- The Centers for Disease Control and Prevention - www.cdc.gov/drugresistance/community/
- The Los Angeles County Department of Health Services Acute Communicable Disease Control Program - www.lapublichealth.org/acd/antibio.htm

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This month we present two articles that show the dangers of antibiotic overuse and how these dangers can be altered with a change in empiric antibiotics.

Outbreak of *Clostridium difficile* Infection in a Long-Term Care Facility: Association with Gatifloxacin Use

R. Gaynes, D. Rimland, E. Killum, H. K. Lowery, T. M. Johnson II, G. Killgore, and F. C. Tenover. Clin Infect Dis 2004; 38:640-5.

This outbreak investigation was conducted to determine the cause of an increased rate of *Clostridium difficile*-associated diarrhea (CDAD) in a long-term care facility. Results of a case-control study showed that the increase of CDAD cases was associated with a formulary change from levofloxacin to gatifloxacin. The rate per 1,000 patient-days increased from 0.44 for the study period of levofloxacin use to 1.32 for the study period of gatifloxacin substitution ($p<.01$). The rate of CDAD decreased to 0.5 cases per 1,000 patient-days after a change back to levofloxacin therapy. The authors note that risk factors associated with CDAD in a long-term care facility may differ from other settings such as acute care hospitals.

Clindamycin, Cephalosporins, Fluoroquinolones, and *Clostridium difficile*-Associated Diarrhea: This is an Antimicrobial Resistance Problem

D. N. Gerding. Clin Infect Dis 2004; 38:646-8.

The following editorial commentary reviews a historical timeline of CDAD risk associated with clindamycin and cephalosporin treatment leading up to the increased but variable CDAD risks associated with fluoroquinolone use. Studies have suggested, but have not proven, the association of CDAD with the disruption of colonic flora by anaerobic activity of specific antimicrobials. However, the author suggests that additional factors of fluoroquinolone resistance in *C. difficile* and proliferation of these specific clones in specific hospitals are the critical events leading to CDAD outbreaks. As cited in Gaynes et al., the success of decreasing CDAD rates by substitution of related fluoroquinolones (gatifloxacin to levofloxacin) remains to be seen elsewhere.

The above article and editorial commentary are available at: www.journals.uchicago.edu/CID/journal/contents/v38n5.html

Clinical practice guidelines and other resources are available online at:

- Infectious Diseases Society of America - www.idsociety.org
- Clinical Practice Guidelines -www.journals.uchicago.edu/IDSA/guidelines/
- The California Medical Association (CMA) Foundation - www.aware.md/resource/index.asp
- Clinical Practice Guidelines Compendium (Pediatric and Adult) - www.aware.md/clinical/clinical_guide.asp
- Centers for Disease Control and Prevention - www.cdc.gov/drugresistance/community/
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THE PUBLIC'S HEALTH

is published by:

COUNTY OF LOS ANGELES
DEPARTMENT OF HEALTH SERVICES
Public Health

313 North Figueroa Street, Room 212
Los Angeles, California 90012

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Trends in Antimicrobial Drug Development: Implications for the Future

Spellberg B, Powers JH, Miller LG, Edwards JE. Clin Infect Dis. 2004;38:1279-1286*

It is especially important that doctors assist public health efforts by prescribing judiciously and educating patients on the appropriate use of antibiotics since drug companies are cutting back on the development of new antibiotics.

The emergence of multidrug resistance and consequential limited antibiotic choices illustrate the need to expand research and development for new antibacterial agents. However, pharmaceutical and biotechnology companies have shifted research efforts away from antibacterial agents for several reasons; for instance, medications used for chronic conditions are more profitable. An evaluation of the U. S. Food and Drug Administration's (FDA) databases confirms this declining trend in the development of new antibacterial agents. FDA approval of new antibacterial agents has decreased by 56% over the past 20 years (1998-2002 vs. 1983-1987). And the prospects of future development of new antibiotics are bleak — only 6 of 506 drugs currently in development by the major drug companies are antibacterial agents.

The authors recommend several strategies to increase the research and development of new antibacterial agents including:

- establishing partnerships between research and development programs and government, academia and industry
- streamlining efforts in the drug approval process that do not compromise safety and efficacy standards
- creating government contracts to develop antibacterials to meet specific national needs, and
- creating legislation to provide economic incentives.

* Article available online at: www.journals.uchicago.edu/CID/journal/issues/v38n9/33161/33161.html

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- Clinical Practice Guidelines - www.journals.uchicago.edu/IDSA/guidelines/
- California Medical Association (CMA) Foundation - www.aware.md/resource/index.asp
- Clinical Practice Guidelines Compendium (Pediatric and Adult) - www.aware.md/clinical/clinical_guide.asp
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During this cold and flu season, the potential for unnecessary antibiotic prescribing for viral illnesses is at its greatest. Due to the flu vaccine shortage this season, this may greatly impact the extent of illness, and as such, the number of people who will erroneously request antibiotics. Despite good intentions, physicians lack knowledge about appropriate antibiotic use even when they are aware that antibiotic resistance is a problem in their own facility. Furthermore, many physicians continue to jeopardize the health of patients by not complying with hand hygiene recommendations—this increases patients' risk to life threatening antibiotic-resistant infections.

A Survey of Knowledge, Attitudes, and Beliefs of House Staff Physicians From Various Specialties Concerning Antimicrobial Use and Resistance.

Srinivasan A, Song X, Richards A, Sinkowitz-Cochran R, Cardo D, Rand C. Arch Intern Med. 2004 Jul 12;164(13):1451-6. Available at: www.archinte.ama-assn.org/cgi/content/full/164/13/1451

In an effort to improve antimicrobial use and prevent resistance, physicians at a university teaching hospital were surveyed to assess their knowledge, attitudes and behaviors antimicrobial use and resistance. Medical residents were significantly more knowledgeable than other groups. Despite overall low scores, the majority of physicians wanted more education on antimicrobials (90%) and more feedback on antimicrobial selections (67%). Physicians were well aware of the problem of antimicrobial resistance and believed that appropriate antimicrobial use is necessary—88% agreed antibiotics are overused in general and 72% also agreed that this was the case at their institution; 96% agreed that hospitals face serious problems with antibiotic resistance and 93% agreed that their hospital faces these same problems; 97% agreed that better use of antibiotics would reduce resistance. The authors recommend that tailored programs that target different physician specialties may be more effective in supporting antimicrobial education.

The CDC offers important tools for preventing antimicrobial resistance in health care settings, such as hospitals and long-term care facilities. For more information, visit: www.cdc.gov/drugresistance/healthcare

Hand Hygiene among Physicians: Performance, Beliefs, and Perceptions.

Pittet D, Simon A, Hugonnet S, Pessoa-Silva CL, Sauvan V, Perneger TV. Ann Intern Med. 2004 Jul 6;141(1):1-8.

Despite the recommendation that hand washing is important to reduce the risk of infection and disease transmission, observational studies continue to show low adherence to this simple practice in health care settings. Physician adherence to hand hygiene practices in a large university hospital averaged 57% overall. Adherence was higher when physicians were aware of being observed (61%; n=117) than when they were not aware of being observed (44%;n=46). Low adherence was associated with busy workloads, performance of activities associated with high risks for cross contamination, and being in technical specialties (such as surgery and anesthesiology). High adherence was associated with easy access to hand-rub solutions, positive attitudes towards hand hygiene after patient contact, and the belief of being a positive role model for other colleagues. The authors support hand hygiene promotion efforts on these factors associated with high adherence, especially towards physicians working in technical specialties.

For CDC guidelines and materials to promote hand hygiene practices at your health care facility, visit: www.cdc.gov/handhygiene

Clinical practice guidelines and other resources are available online at:

- Infectious Diseases Society of America – www.idsociety.org
- Clinical Practice Guidelines – www.journals.uchicago.edu/IDSA/guidelines/
- California Medical Association (CMA) Foundation - www.aware.md/resource/index.asp
- Clinical Practice Guidelines Compendium (Pediatric and Adult) - www.aware.md/clinical/clinical_guide.asp
- Centers for Disease Control and Prevention – www.cdc.gov/drugresistance/community/
- Los Angeles County Department of Health Services Acute Communicable Disease Control Program – www.lapublichealth.org/acd/antibio.htm